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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/950,082	09/12/2001	Craig A. Rosen	PS-804	9299

22195 7590 03/22/2004

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INTELLECTUAL PROPERTY DEPT.
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EXAMINER	
SHEINBERG, MONIKA B	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/950,082	ROSEN ET AL.	
	Examiner	Art Unit	
	Monika B Sheinberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U S C § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15 and 24-57* is/are pending in the application.

4a) Of the above claim(s) *15* is/are withdrawn from consideration.

5)☒ Claim(s) *26 and 32* is/are allowed.

6)☒ Claim(s) *24,25,27-31 and 33-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *15 and 24-57* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: *Detailed Action*.

DETAILED ACTION

Response to the Amendment filed: 10 December 2003

1. Applicants' arguments, filed 10 December 2003, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. The cancellation of claims 1, 8, 13, 17-20 and 22 and the amendments made to claims 36 and 43 are acknowledged. Claims 15 and 24-57 are pending.

3. Claim 15 remains withdrawn from consideration.

4. Claims 24-57 with respect to SEQ ID NO: 764 and deposit HLYEU59 have been examined.

Priority

5. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged to be March 26, 1999 due to the disclosure of SEQ ID NO: 764 and clone HLYEU59 to their corresponding to sequences (SEQ ID NO: 81 and gene 21).

MAINTAINED REJECTIONS

Claim Rejections - 35 USC § 101 /112

6. It is to be noted that the rejection of claims 24-57 under 35 U.S.C. 101/112-1st paragraph based on utility has been hereby withdrawn due to the supported differentiated expression level of chronic lymphatic leukemia in the spleen in comparison to all of the listed cell types/tissues listed in table 4 which includes normal spleen.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. The rejection of claims 24, 25, 27-31, 33-35 and 50-57 is maintained and reiterated under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

9. WRITTEN DESCRIPTION: Claims 24, 25, 27-31, 33-35 and 50-57 are directed to a predicted polypeptide sequence. Applicants have not experimentally isolated the claimed 'isolated protein', but merely base the description on homology and predictive analyses such as the region of amino acids that may carry characteristics such as signal peptide and secreted peptide.

The claims directed to encompass proteins corresponding to sequences of 90% or 95% identity to the overall or portion of SEQ ID NO: 764 (claims 36-49) have been withdrawn from the instant rejection because claim 36 and 43 have been amended to include functional language. However claims 24, 25, 27-31, 33-35 and 50-57 still encompass sequences not described by the specification for reasons of record. Although the sequence itself distinguishes the structural features of the nucleic acid, sequences, beyond exact identity (be it in entirety or to contiguous fragments) of the elected SEQ ID NO: 764, are included but not disclosed as to written description. Each variation of the non-identical, results in a new and independent sequence that does not reliably result in similar or identical biological activities as result for example from altered folding patterns. For example, it would have been known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. As discussed above, in the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent

mutations having no effect. Thus the instant claims are directed to encompass peptide sequences that correspond to sequences from other species, mutated fragment sequences, allelic variants, splice variants, and so forth. None of these additional sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Response to Arguments

10. On page 27, 3rd paragraph: Applicants assert that "while applicant must 'blaze marks on trees,' rather than 'simply [provide] the public with a forest of tress,' an Applicant is not required to explicitly describe each of the trees in the forest" [in citing *Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 54 USPQ2d 1227 (Fed. Cir. 2000)]. This argument has been thoroughly reviewed but is not found to be persuasive because the specification does not reflect possession of mutants, variants, or homologs of SEQ IDNO: 764 from any source by merely disclosing the sequence of SEQ ID NO: 764 and general descriptions on how to alter it. For example, isolation of SEQ ID NO: 764 from the deposit HLYEU59 does not reflect possession of mutants or variants of SEQ ID NO: 764, nor possession of peptides of any magnitude and/or content. The sequences encompassed by the claims are of any magnitude and/or content that comprise at least the specified region of SEQ ID NO: 764 are included in the above: as seen in claim 24, for example, "an isolated protein *comprising* amino acid residues 25-45 of SEQ ID NO: 764." The claims remain encompassing sequences that are not described by the specification. For example, it would have been known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. Any variation in amino acid sequence results in a new and independent sequence that does not reliably result in similar or identical biological activities as result for example from altered folding patterns. Flanking amino acids are included within the mutations of an amino acid sequence that can alter the folding pattern. While one of skill in the art could argue that the claimed genus of polypeptides is adequately described since one can isolate these peptide sequences using the polypeptide/polynucleotide structures disclosed in the instant application or the prior art, the state of the art teaches that sequence comparison alone should not be used to determine a protein's function and that small amino acid changes can drastically change the function of a

polypeptide. Bork [Genome Research, 10: 398-400 (2000)] teaches protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). Van de Loo et al. [PNAS 92; 6743-6747 (1995)] teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* were found to be hydroxylases once tested for activity. Seffernick et al. [J. Baceriol. 183 (8); 2405-2410 (2001)] teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al. [Science 282: 1315-1317 (1998)] teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydroxylase and as few as six amino acid substitutions can transform a hydroxylase to a desaturases. Thus absent factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. The genus of peptides comprised by the claim is a large variable genus, which can potentially encode proteins of diverse functions and encompass peptide sequences that correspond to sequences from other species, mutated fragment sequences, allelic variants, splice variants, and so forth. None of these additional sequences meet the written description provision of 35 USC 112, first paragraph. The specification only discloses a single species of the genus, i.e. the polypeptide of SEQ ID NO: 764, which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116.)

With the exception of a substantially purified amino acid molecule comprising of the sequence of SEQ ID NO: 764, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The amino acid sequence itself is

required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997);
>
> *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Accordingly, the specification does not provide a written description of the invention of claims 24, 25, 27-31 and 33-35.

11. On page 28, 3rd paragraph: Applicants argue that applicants were in possession of the polypeptides encompassed by the claims because the polynucleotides encoding the claims polypeptides were submitted within deposit HLYEU59, while the specification described how to isolate said polypeptide. This argument has been thoroughly reviewed but is not found to be persuasive because of reasons stated above in section #10; i.e. isolation of SEQ ID NO: 764 from the deposit HLYEU59 does not reflect possession of mutants or variants of SEQ ID NO: 764, nor possession of peptides of any magnitude and/or content.

12. On pages 27-28, bridging paragraph: Applicants assert that Examiner has not met the burden of presenting "evidence or reasons why one skilled in the art would not reasonably

conclude that Applicants possessed the subject matter as of the priority date of the present application." This argument is not found persuasive because of the reasons Examiner presented with respects to the unpredictability of characterizing the structural and functional components of the biomolecule in sections #9 and further in #10.

13. On page 28, 4th paragraph: Applicants further assert that the amendment to the claims 36 and 43 "wherein said protein activates transcription in immune cells" overcomes the Examiner's statement that "[e]ach variation of the 5% or 10% non-identical, results in a new and independent sequence that does not reliably result in similar or identical biological activities as result for example from altered folding patterns". The instant argument is moot as these claims and those dependent therefrom, are no longer included within this rejection. The claims have been amended to include functional language.

14. On page 29, 2nd-3rd paragraph: Applicants further assert that "the claimed invention is specifically directed to human secreted proteins (*see*, Abstract), and in particular, polypeptides corresponding to the selected clone of the invention HLYEU59 (3rd paragraph). This arguments has been thoroughly reviewed yet is not found persuasive because this limitation is not within the claims. Further, even if they were, the specification has not taught what distinguishes a "human" variant or fragment of SEQ ID NO: 764 from a variant or fragment from another species.

15. On page 29, 3rd paragraph: Applicants assert that the disclosure provides adequate written description support for the mutated fragment sequences, allelic variants sequences or splice variants because "Applicants have provided the core structural feature of the polypeptides of the inventions, namely SEQ ID NO: 764" (3rd paragraph). This argument has been thoroughly reviewed but is not found to be persuasive because of reasons stated above in section #10.

16. Therefore, the arguments are non-persuasive to overcome the rejection.

NEW REJECTIONS AS NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

17. The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 36-49 are rejected as necessitated by amendment under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention.

19. In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. j 1 12, first paragraph, have been described. They are:

> *Nature of the invention,*
> *State of the prior art,*
> *Predictability or lack thereof in the art,*
> *Amount of direction or guidance present,*
> *Presence or absence of working examples,*
> *Breadth of the claims,*
> *Quantity of experimentation needed, and*
> *Level of the skill in the art.*

The Nature of the Invention and the Breadth of the claims

20. The nature of the invention is the isolated protein of SEQ ID O: 764 or the peptide encoded by the HLYEU59 cDNA contained in ATCC Deposit No. 203957, secreted portions thereof, and portions of the whole peptide or partial peptide that corresponds to the amino acid sequence of SEQ ID NO: 764. In addition, the clone is primarily expressed in the spleen of humans afflicted with chronic lymphocytic leukemia (Table 1B, p. 235), and the bioactivity of the instant peptide is "activation of transcription through the AP1 response element" (Table 1E, p. 924). The breadth of the claims is very broad and encompasses mutants, variants, or homologs of SEQ IDNO: 764 from any source and any magnitude and/or content.

The state of the Prior Art and the Predictability or Lack Thereof in the Art

21. The prior art does not teach what the specification fails to teach in regards to how the skilled artisan can activate transcription of an undefined product in immunes cells with the claimed proteins that encompass peptides corresponding to sequences of 90% or 95% identity to the overall or portion of SEQ ID NO: 764 and sequences of any magnitude and/or content. The specification fails to teach or suggest which specific amino acids can be altered by the skilled artisan without altering or destroying the function of activating transcription, or activating transcription in immune cells. Each variation results in a new and independent sequence that does not reliably result in similar or identical biological activities of the peptide in its entirety. The sequences encompassed by the claims are of any magnitude and/or content that comprise at least the specified region of SEQ ID NO: 764, and thus include flanking amino acids which are inclusive of mutations of an amino acid sequence that can alter its folding pattern. The state of the art teaches that sequence comparison alone should not be used to determine a protein's function and that small amino acid changes can drastically change the function of a polypeptide. It is known for proteins, for example, that even a single amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. Any variation in amino acid sequence results in a new and independent sequence that does not necessarily reliably result in similar or identical biological activities as the as result, for example, from altered folding patterns. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. In the instant case, the functional activity of the claimed sequence homologies and sequences containing only fragments of the entire sequence SEQ ID NO: 764, is unpredictable, thus unreliable, in maintaining the same bioactivity of the entire SEQ ID NO: 764 and the claimed fragment or variant peptide, and therefore lacks support regarding enablement. For further clarification of the lack predictability, the state of the art teaches that sequence comparison alone should not be used to determine a protein's function and that small amino acid changes can drastically change the function of a polypeptide. Bork [Genome Research, 10: 398-400 (2000)] teaches protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). Van de Loo et al. [PNAS 92; 6743-6747 (1995)] teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* were found to be hydroxylases once tested for activity. Seffernick et al. [J. Baceriol. 183 (8); 2405-2410 (2001)] teaches that two naturally occurring Pseudomonas enzymes having

98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al. [Science 282: 1315-1317 (1998)] teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydroxylase and as few as six amino acid substitutions can transform a hydroxylase to a desaturases. Thus level of unpredictability is high in the art.

In addition, the state of the art post-filing demonstrate the signaling pathways that induce or inhibit AP1 transcriptional activation are unpredictable and highly variable in the AP1 complex and response element such as its activation can be both oncogenic and anti-oncogenic all of which is dependent upon a multitude of factors within the composition and its cellular environment. The AP1 transcription factor made up of other proteins wherein variations in the make up of the proteins JUN, FOS, ALF and MAF can greatly affect the functional responses as greatly as the presence or absence of external stimuli in the cellular environment such as growth factors, cytokines, neurotransmitters, polypeptide hormones, cell-matrix interactions, bacterial and viral infections, and a variety of physical and chemical stresses. [See Shaulian et al. Nature Cell Biology, 2002; and Eferl et al. Nature Reviews Cancer, 2003]. Therefore a skilled artisan would not know which fragment or variant peptide of SEQ IDNO: 764 would be responsible in activating transcription in immune cells.

The Amount of Direction or Guidance Present and the Presence or Absence of Working Examples

22. The specification teaches that the bioactivity of the claimed peptide is the "activation of transcription through AP1 response element in immune cells (such as T-cells)"(table 1B, p. 924, 4th column). The specification fails to teach how this correlates to how to make or use the claimed peptides, whether they are a transcription factor; how it's involved within a cascade of signals that result in AP1 activation; how is it involved in transcription; what is it activating to transcribe. The exemplenary activity assays listed in Table 1E (5th column) do not teach how the peptides would be used in these assays. The prior art does not teach what the specification fails to teach or suggest, such as what role the claimed protein variants play in the highly variable cascade of factors that influence transcription activation at various degrees that involve the AP1 complex or response element. The specification suggests a correlation to transcription activation

of an unknown product, 'through' the AP1 response element in immune cells wherein, for example, the claimed variant peptides may be assessed for their ability to modulate growth and any other cell functions however such broad and general terms as 'growth' or 'other cell functions' that are entailed does not enable the skilled artisan to know how or where to direct the use of the claimed peptide in such an assessment. The specification also suggests the use of the claimed peptides to test AP1 response element activity yet fails to teach or suggest how the skilled artisan would apply the claimed peptides in such a test. The exemplenary assays referenced are generally applied to activity and behavior studies which do not teach the skilled artisan to determine the claimed peptides' direct or indirect interaction and/or function with the AP1 response element or complex in its transcriptional activation. None of the references listed exemplify how to correlate the data potentially generated by the application of such assays to the undefined differential expression demonstrated in the spleen cells affected by chronic lymphocytic leukemia. Applicants incorporated references for exemplification of the AP1 and T cell activity assays. With regards to the references incorporated by reference, applicant has not indicated what part of these references teach what to do with the peptide/how to use the peptide; how and in what fashion is the peptide being used to 'test AP1-response element activity' as directed to what reason; what ability of the peptide is being 'assessed' by the exemplenary assays for modulation of cell growth and/or other cell functions? The articles referenced have been reviewed (Fraser et al., 1999; Chang et al, 1998; Rellahan et al, 1997; Cullen et al., 1992; and Berger et al.; 1988). However the references are general assays that fail to teach how these assays are to be utilized with the claimed peptide and state that there is complexity and a high number of elements involved in such signaling pathways. They teach assays that potentially do or do not activate AP1 along with other signal pathways with respect to T cell proliferation and differentiation in a general fashion; none specific to how these assays are utilized with the claimed peptides or how such assays would be used to make the claimed peptides. Fraser teaches a general characterization of the T-cell to AP1 transcriptional activation pathway, which is unpredictable due to several key transcription factors important in this regulatory pathway. Chang teaches that although the proteins demonstrated were involved in AP1 transcriptional activation, their association to the cascade of events is unknown and requires further research. Chang further states the lack of knowledge in the immediate biochemical effects from induction;

in addition to if and how the protein cooperates or interacts with other molecules or stimuli in the cellular environment (p. 4992, 1st column, 2nd paragraph), thereby suggesting the required further research and experimentation as unpredictable. Rellahan demonstrates the lack of understanding the functional role of a protein somehow involved in regulating T-cell receptor mediated signal transduction pathways in conjunction with the complex and multivariate signaling pathway of Ras and AP1 activation. Cullen and Berger teach alternate reporter genes for gene expression quantitation. Cullen and Berger fail to exemplify any protein activity assay or correlation to transcription activation in T cells or immune cells, or transcription activation through the AP1 response element. There are many factors to consider for transcriptional activation in T cells though AP1 activation such as the inhibition or activation of different receptors, the internal environment of the cell and how certain stimuli will mediate different pathways. Ideally, the use of examples in a given specification typically serve to demonstrate at least the critical limitations and/or requirements in order to make/use an invention. However, the examples are generic in nature and not specific to the claimed sequences containing only fragments of SEQ ID NO: 764 and/or 90-95% homologies to the partial or whole sequence of SEQ ID NO: 764.

Quantity or Experimentation needed and Level of the Skill in the Art

23. The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine which portions of SEQ ID NO: 764 are critical to its bioactivity and then determine if portions containing such regions would maintain the same bioactivity of transcription activation as the full peptide sequence (i.e. SEQ ID NO: 764). In addition, the skilled artisan would need to determine how to use the claimed variant peptides in i.e. increasing induction or inhibition of AP1 transcriptional activation, which AP1 complex is being activated, then if activated which signal cascades are involved, which tissue/cellular environments are affected and what stage of the cancer is correlated (in regards to the leukemia). One of skill in the art would then have to perform undue experimentation to determine which mutations or alterations (including magnitude and content) would result in a the claimed peptides maintaining the same bioactivity as the entirety of SEQ ID NO: 764. Due to the level of skill in the art being high and the unpredictability in the art being even higher, each embodiment of the invention is required to be individually assessed for functional activity. Such analysis is replete with

unpredictable trial and error analysis and is considered undue. Thus, the specification fails to provide sufficient enablement for how to make or use the broadly claimed variant peptides. As a result necessitating one of skill to perform an exhaustive research and experimentation determine how to make or use the instantly claimed peptides.

Allowable Subject Matter

24. Claims 26 and 32 are allowed. The following is a statement of reasons for the indication of allowable subject matter: claims 26 and 32 are free of the prior art and have overcome the 35 U.S.C. 101 and 112 issues due to the supported differentiated expression level of chronic lymphatic leukemia in the spleen in comparison to all of the listed cell types/tissues listed in table 4 which includes normal spleen.

Conclusion

MAINTAINED

- The rejection of claims 24, 25, 27-31, 33-35 and 50-57 is reiterated and maintained under 35 U.S.C. 112, first paragraph – written description.

NEW

- Claims 36-57 are rejected as necessitated by amendment under 35 U.S.C. 112, first paragraph – enablement.

ALLOWABLE

- Claims 26 and 32 are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The central **Fax number is (703) 872-9306**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (571) 272-0749. The examiner can normally be reached on Monday-Friday from 9 A.M to 5 P.M. If attempts to reach the examiner by telephone are unsuccessful, the primary examiner in charge of the prosecution of this case, Jehanne Sitton, can be reached at (571) 272-0752. If attempts to reach the examiners are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Chantae Dessau, whose telephone number is (571) 272-0518, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

March 18, 2004
Monika B. Sheinberg
Art Unit 1634
MBS

Jehanne Sitton
JEHANNE SITTON
PRIMARY EXAMINER
3/18/04